

C. Remarks

The claims are 48-61, 63-66, 73-77, 79 and 80, with claims 48 and 63 being independent. Claims 54-61 and 75-77 have been withdrawn from consideration by the Examiner as being drawn to non-elected subject matter. Claims 48, 49 and 63 have been amended; specifically, each of the noted claims has been amended to replace the term “subject” with the phrase --human subject--. Applicant submits that no new matter has been added as this amendment is fully supported by the application as originally filed, e.g., at page 5, line 8-14. Reconsideration of the present claims is respectfully requested.

Claims 48-53, 63-66, 73, 74, 79 and 80 stand rejected under 35 U.S.C. §112, second paragraph, as being allegedly indefinite for inclusion of the phrase “a subject”. Applicant respectfully traverses this rejection. It is clear from a reading of the specification that what is intended by the phrase “a subject” is a human subject having a bone fracture. Applicant further submits, contrary to the Examiner’s position, that one of ordinary skill in the art could readily ascertain and interpret the metes and bounds of the patent protection desired without further amendment of the claims; indeed, there is simply no basis upon which one of ordinary skill in this art could rely to interpret “subject” in these claims to include a non-biological system, given the requirement of a subject with a fracture. However, in an effort to expedite prosecution of this case, Applicant has amended each of claims 48, 49 and 63 to specify that the subject is a human subject. Accordingly, Applicant respectfully requests withdrawal of the §112 rejection.

Claims 48-52, 63 and 64 stand rejected under 35 U.S.C. §102(b) as being anticipated by Yates (U.S. Patent No. 5,646,134). Applicant respectfully traverses this rejection.

The present invention is specifically directed to a method of promoting bone growth or new bone formation at a fracture site by administering a drug containing at least one bisphosphonate. Other embodiments of the invention are directed to the administration of at least two bisphosphonates. Importantly, according to the methods of the present invention, an amount of at least one bisphosphonate effective to promote bone growth or new bone formation at a fracture site is administered to a human subject with a fractured bone. This key feature is not disclosed or suggested in any way by Yates.

Yates is directed to a therapy for preventing periprosthetic bone loss by the administration of a bisphosphonate bone resorption inhibitor. While Yates expresses a desire for the development of “localized controlled/extended release dosage forms of bone growth promotant” (col. 1, lines 33-35), Yates does not hold out its bisphosphonate therapy as such a bone growth promotant. Instead, Yates consistently characterizes its use of the bisphosphonate alendronate as “specifically prevent[ing] bone resorption in the periprosthetic bone area of an orthopedic implant device” (col. 2, lines 35-38). Yates further teaches the use of an “osteogenically effective amount” of bisphosphonate as an amount to inhibit bone resorption (prevention of bone loss, inhibition of removal of existing bone) in the periprosthetic bone area of a medical implant device (col. 3, lines 18-29). Yates provides no teaching with regard to the use of a bisphosphonate at a fracture site.

The fact that a bisphosphonate can be useful in preventing bone loss in an area of bone which is in contact with or in the immediate proximity of a medical implant device does not imply its usefulness to promote bone growth or new bone formation at a fracture site. This point is bolstered by the background section of Yates. Therein Yates describes the known uses of bisphosphonates, primarily as therapeutic agents in the treatment of osteoporosis. Yates further implies that the success of bisphosphonates in the osteoporosis context says nothing as to the use of bisphosphonates in the context of device implants. Likewise, the success of bisphosphonates in the implant context says nothing as to the use of bisphosphonates in the context of a bone fracture.

For the above reasons, Applicant submits that Yates fails to disclose or suggest all the key features of the present invention, namely the use of a bisphosphonate to promote bone growth or new bone formation at a fracture site. Withdrawal of the §102 rejection is respectfully requested.

Claims 48-53, 63, 73 and 79 stand rejected under 35 U.S.C. §102(a) as being unpatentable over Ke (U.S. Patent No. 6,352,970). Applicant respectfully traverses this rejection.

As noted above, the present invention is specifically directed to a method of promoting bone growth or new bone formation at a fracture site by administering a drug containing at least one bisphosphonate. Other embodiments of the invention are directed to the administration of at least two bisphosphonates. Importantly, according to the methods of the present invention, an amount of at least one bisphosphonate effective to promote bone growth or new bone formation at a fracture site is administered to a human

subject with a fractured bone. This key feature is not disclosed or suggested in any way by Ke.

Ke focuses on the use of leptin or a leptin mimetic (at times in combination with estrogen, a selective estrogen receptor modulator or a bisphosphonate) for treating low bone mass or bone fracture. Since Ke refers, in general, to the use of leptin alone for these purposes, one of ordinary skill in this art would not, upon reading Ke, have any reason to believe that a bisphosphonate on its own would be effective for the purposes set forth therein.

Moreover, Ke does not teach or suggest anywhere that bisphosphonates might be used for promoting bone growth or new bone formation at a fracture site. In fact, Ke explicitly teaches against such a notion. At column 2, lines 14-18, Ke states: "All approved therapies and clinically advanced candidates including . . . bisphosphonates . . act to prevent bone loss by inhibiting bone resorption, but these agents cannot restore bone mass." Given this disclosure, one of ordinary skill in the art would surely not be motivated to pursue a method of promoting bone growth or new bone formation which centered on the administration of a bisphosphonate.

In sum, it is clear that Ke does not render the presently claimed invention obvious. Ke simply fails to disclose or suggest certain key features of the present invention, namely the administration of an amount of at least one bisphosphonate which is effective to promote bone growth or new bone formation at a fracture site. Accordingly, Applicant respectfully requests withdrawal of the §103 rejection.

Claims 48-50, 52, 53, 63-66, 74 and 80 stand rejected under 35 U.S.C. §102(b) as being unpatentable over Geddes (WO 93/11786). Applicant respectfully traverses this rejection.

As noted above, the present invention is specifically directed to a method of promoting bone growth or new bone formation at a fracture site by administering a drug containing at least one bisphosphonate. Other embodiments of the invention are directed to the administration of at least two bisphosphonates. Importantly, according to the methods of the present invention, an amount of at least one bisphosphonate effective to promote bone growth or new bone formation at a fracture site is administered to a human subject with a fractured bone. This key feature is not disclosed or suggested in any way by Geddes.

Geddes is directed to methods of treating osteoporosis. In fact, Geddes teaches the treatment of osteoporosis only with combinations of a bisphosphonate and parathyroid hormone. Since Geddes refers, in general, to the use of such a combination for these purposes, one of ordinary skill in this art would not, upon reading Geddes, have any reason to believe that a bisphosphonate on its own would be effective for the purposes set forth therein. What is more, Geddes provides no teaching at all with regard to the use of a bisphosphonate at a fracture site. The fact that a bisphosphonate can be useful in the treatment of osteoporosis does not imply its usefulness to promote bone growth or new bone formation at a fracture site. What is more, Geddes' example of treating a male with a history of atraumatic fractures with a combination of parathyroid hormone and a

bisphosphonate does not suggest treatment of a human subject with a fracture with a bisphosphonate alone.

For the above reasons, Applicant submits that Geddes fails to disclose or suggest all the key features of the present invention, namely the use of a bisphosphonate to promote bone growth or new bone formation at a fracture site. Withdrawal of the §102 rejection is respectfully requested.

Claims 48-51, 63 and 64 stand rejected under 35 U.S.C. §102(b) as being unpatentable over Goodship (*Annals of Oncology* 5 (Suppl. 7) S53-S55, 1994). Applicant respectfully traverses this rejection.

As noted above, the present invention is specifically directed to a method of promoting bone growth or new bone formation at a fracture site by administering a drug containing at least one bisphosphonate. Other embodiments of the invention are directed to the administration of at least two bisphosphonates. Importantly, according to the methods of the present invention, an amount of at least one bisphosphonate effective to promote bone growth or new bone formation at a fracture site is administered to a human subject with a fractured bone. This key feature is not disclosed or suggested in any way by Goodship.

Goodship, while being directed to the use of a bisphosphonate to modulate fracture repair, finds only that bisphosphonates have no adverse effects on the restoration of the mechanical integrity of a long bone after fracture or on fracture healing. Goodship tests the hypothesis that bisphosphonates modulate the remodelling phase of fracture repair. Such findings are clearly different from a teaching of the use of a bisphosphonate to

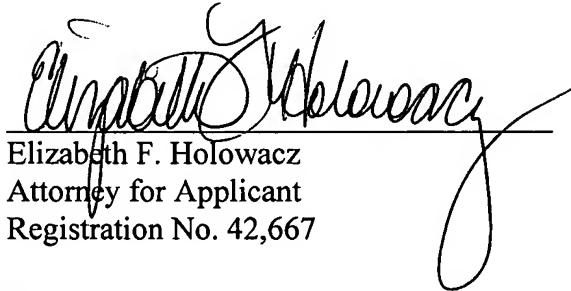
promote bone growth or new bone formation. Goodship premises increased bone mineral content upon bisphosphonates' ability to affect the properties of developing bones mediated by their influence on the coupling between bone formation and resorption, their influence on osteoclast recruitment mechanisms and cytokine production, inhibition of calcium phosphate precipitation and other as yet unexplained mechanisms. Goodship also acknowledges the limited work that has been done to explore the role of bisphosphonates in fracture repair (p. S53).

For the above reasons, Applicant submits that Goodship fails to disclose or suggest all the key features of the present invention, namely the use of a bisphosphonate to promote bone growth or new bone formation at a fracture site. Withdrawal of the §102 rejection is respectfully requested.

In view of the foregoing amendments and remarks, favorable reconsideration and passage to issue of the present case is respectfully requested. Should the Examiner believe that issues remain outstanding, the Examiner is respectfully requested to contact Applicant's undersigned attorney in an effort to resolve such issues and advance the case to issue.

Applicant's undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,


Elizabeth F. Holowacz
Attorney for Applicant
Registration No. 42,667

FITZPATRICK, CELLA, HARPER & SCINTO
30 Rockefeller Plaza
New York, New York 10112-3801
Facsimile: (212) 218-2200

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